REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

The claims have been amended to define the invention with additional clarity. The claims as presented are fully supported by an enabling disclosure.

Claims 24 and 34 stand rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

The Examiner contends that claim 24 is indefinite because it is unclear whether the claim is directed to:

1. an asparaginase or a vector, or
2. an asparaginase obtained by expressing a polynucleotide or by expressing a vector comprising said polynucleotide.

Applicants submit that, in fact, one skilled in the art would readily appreciate that it is the latter. Nonetheless, in order to avoid any doubt, claim 24 has been revised to define the invention with yet additional clarity.

The Examiner also considers claim 34 to be indefinite because it refers to an asparaginase with 95% homology to SEQ ID NO:3, which has asparaginase activity. To remove any perceived redundancy, the claim has been revised to delete the phrase "and the asparaginase has asparaginase activity".

Reconsideration is requested.

Claims 24, 32 and 40 stand rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement. Withdrawal of the rejection is in

order in view of the revision of the claim to include the washing conditions. Reconsideration is therefore requested.

Claim 23 stands rejected under 35 USC 112, first paragraph, as allegedly lacking written description. Withdrawal of the rejection is in order for the reasons that follow.

The Examiner contends that the description provides no teaching of how the skilled person should obtain sequence homologues of SEQ ID NO:3 that maintain asparaginase activity. Applicants respectfully disagree.

The portion of the description entitled "Functional equivalents" (page 18 to 23) provides several examples of how the artisan could obtain functional equivalents of SEQ ID NO:3. For instance, it is indicated how "conservative substitutions" can be made. This refers to replacement of an amino acid for another amino acid with similar side chain. Further, it is explained, with reference to Bowie, J.U. et al, Science 247:1306-1310 (1990), how to make phenotypically silent amino acid substitutions. The same type of illucidation is provided as regards so-called orthologues of the protein ASPA01. Therefore, the skilled person would not have difficulty in appreciating highly homologous sequences of SEQ ID NO:3 which still maintain asparaginase activity.

The Examiner maintains that the art clearly demonstrates that even small changes in the amino acid sequence can result in changes in the enzymatic activity and, therefore, render protein engineering totally unpredictable. The Examiner refers to J. Bacteriol. 183(8): 2405-2410, 2001, where two naturally occurring enzymes having 98% sequence identity show different enzymatic activities, as an example to support the assertion.

However, as indicated in the previous response, the same article negates the conclusion that protein engineering would be totally unpredictable: Page 2409, 1st column, lines ~24-26

states that "the present finding that proteins with >98% sequence identity catalyze different reactions in different metabolic pathways is highly exceptional" (underlining added). The fact that Branden (of record) also warns that sometimes surprises can occur, does not alter the fact that he also states that: "...**protein engineering,** by which we mean mutating the gene of an existing protein in an attempt to alter its function in *a predictable way*" (see the last 4 lines of the first paragraph, emphasis added). In fact, it goes without saying that the person skilled in the art is capable of mutating a gene in a predictable way, especially when staying within the 95% homology frame, because, otherwise, the field of protein engineering would not even exist.

Withdrawal of the rejection is requested.

Claims 22-25, 32 and 40 stand rejected under 35 USC 112, first paragraph, as allegedly being non-enabled. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

Applicants' specification teaches a person skilled in the art how to make asparaginases according to the invention and to confirm their enzymatic activity. The amount of experimentation required to determine whether an amino acid sequence having at least 90 or 95% sequence identity to SEQ ID NO: 3 OR encoded by a polynucleotide that hybridizes under highly stringent conditions to the complement of SEQ ID NO: 1 or 2 has asparaginase activity would not be undue for skilled artisans familiar with protein engineering.

Withdrawal of the rejection is clearly in order and the same is requested.

Claims 24, 32 and 40 stand rejected under 35 USC 102(b) as allegedly being anticipated by Milton at all. Withdrawal is requested for the reasons that follow.

Milton et al discloses peptide sequences with a level of homology with A. niger asparaginase of ~40%. The Examiner argues that this does not mean that the Milton et al peptide

would not hybridize to the complement of SEQ ID NO:1 or SEQ ID NO:2 under the conditions required in claim 24. The Examiner states that the hybridization can also take place over only a small fraction of the complement of the sequences cited. However, the claim recites "a polynucleotide of SEQ ID NO:1 or SEQ ID NO:2". This means the full length and not part of it. A peptide with a level of 40 % homology would not hybridize with the full length of the polynucleotides of SEQ ID NO:1 or SEQ ID NO:2 and, therefore, does not anticipate claim 24. Accordingly, this document does not teach, nor would it have suggested, the polypeptides of the present claims.

Reconsideration is requested.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 
Mary J. Wilson
Reg. No. 32,955

MJW:tat
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100